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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,556	05/23/2001	Yoshiaki Azuma	TEI-120	9893

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 03/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,556	AZUMA ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *13 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 02/04/04 is acknowledged.

Claims 1-14 are pending.

Newly submitted claims 13-14 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The elected Group II, claims 1-8, now claims 1-12 drawn to a method for inhibiting bone resorption by inhibiting osteoclast formation comprising exposing cells in vitro to ultrasound. Newly submitted claims 13-14 drawn to a method for increasing bone mass , comprising exposing bone to ultrasound *in vivo*.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits.

Accordingly, claims 13 and 14 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-12 drawn to a method for inhibiting bone resorption by inhibiting osteoclast formation comprising exposing cells in vitro to ultrasound are under consideration in the instant application.

2. In view of the amendment, filed 02/04/04 the following rejections remain:

3. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 6 and 8 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is improper to recite " derivatives" in claims 6 and 8, both in line 7, because said claims can read on a mixture of derivatives that are used for the method for inhibiting bone resorption. However, claims 6 and 8 recited the method for inhibiting bone resorption, comprising using one factor. It is suggested that said word be changed to "derivative".

Applicant's arguments, filed 02/04/04 have been fully considered, but have not been found convincing.

Applicant asserts that claims 6 and 8 have been amended to clarify that claims can read on a mixture of inducing factors including derivatives of such factors.

Contrary to Applicants assertion the amended claims still reads on the method for inhibiting bone resorption, comprising using " at least one factor ". It is suggested that the term "derivatives" be changed to "derivative".

5 . The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action maild on 08/26/03. **This is a New Matter rejection**.

Applicant's arguments, filed 02/04/04 have been fully considered, but have not been found convincing.

Applicant asserts that it is clear from the specification and example 3-1 that since osteoclasts have a direct role in bone resorption, inhibition of osteoclast formation inhibits bone resorption.

Contrary to Applicants assertion the issue raised in the previous Office Action was that "a method for inhibiting bone resorption by inhibiting osteoclast formation comprising exposing cells to ultrasound in a culture (i.e. *in vitro*) containing an osteoclast precursor claimed in Claim 1-12 represents a departure from the specification and the claims as originally filed. The passages point by the applicant only support an *in vitro* method for inhibiting osteoclast formation. The example 3-1 only support *in vitro* data for hydroxyapatite-coated disc, not bone resorption *in vitro*.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting osteoclast formation *in vitro*, comprising exposing cells to ultrasound conditions , wherein said conditions are disclosed in overlapping pages 5-6 of the Specification as field, does not reasonably provide enablement a method for inhibiting bone resorption *in vitro*, comprising exposing cells to *any* ultrasound conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action maild on 08/26/03.

Applicant asserts that claimed method is limited to inhibiting osteoclast formation *in vitro.*

The examiner agree that the method for inhibiting osteoclast formation is limited only to *in vitro.* However, the issue raised in he previous office action was that the specification only discloses *in vitro* studies , wherein mouse bone-marrow derived osteoclast precursors (MDBM) were incubated in the presence of soluble osteoclast forming factor (sRANKL) and exposed to ultrasound that results in reduction of the numbers of osteoclasts (see Examples 1-2 in particular). However, said reduction was less than 10-15 % (as shown in Figures I and II) compare to untreated cells and specification does not adequately teach that said reduction would be sufficient to inhibit bone resorption *in vitro.* The example 3-1 only support *in vitro* data for hydroxyapatite-coated disc, not bone resorption. Moreover, bone resorption is a process occurring in patient in *vivo* mediated by the action of several factors including humoral agents, parathyroid hormone calcitonin and vitamin D not *in vitro.* In addition, the Specification disclosed that not *any* ultrasound condition, but very specific one as disclosed on overlapping pages 5-6 should be used (see Page 5-6 of the Specification as field). Luiz. R (US Patent 4,530,360) also teaches hat for most effective treatment with ultrasound a specific ultrasound conditions must be maintained (see entire document, column 2, lines 5-25 in particular). The specification does not adequately teach how to effectively inhibit bone resorption, comprising exposing cells to *any* ultrasound conditions. Murrills R (IDS) teaches that *in vitro* bone resorption assays may not necessarily respond to some agents as adult tissue would and the results from animal tissue may not necessary hold true for human tissues. In addition, these *in vitro* assays may not be representative of the long-term changes in bone metabolism (see entire document, page 1239 in particular). The specification does not teach how to extrapolate data obtained from *in vitro* studies wherein mouse bone-marrow derived osteoclast precursors (MDBM) were incubated in the presence of soluble osteoclast forming factor (sRANKL) and exposed to ultrasound that results in reduction of the numbers of osteoclasts to the development of effective *in vitvo* method for inhibiting bone resorption, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of a method of inhibiting bone resorption *in vitro,* comprising exposing cells to *any* ultrasound conditions. Thus in the absence of working examples or detailed guidance in the specification, the intended uses of a method for inhibiting bone resorption *in vitvo,* comprising exposing cells to *any* ultrasound conditions are fraught with uncertainties.

The specification does not provide sufficient teaching as to how it can be assessed that inhibition bone resorption *in vitro* was achieved after exposing cells to any ultrasound conditions. Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method for inhibiting bone resorption *in vitro* comprising exposing cells to any ultrasound conditions in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher,* 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7 No claim is allowed

8. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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March 1, 2004

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